124. An Eclipsed C(sp^3)–CH_3 Bond in a Crystalline Hydrated Tricyclic Orthoamide: Evidence for C–H···O Hydrogen Bonds

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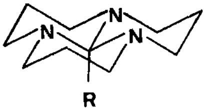
Accurate, low-temperature (81 K) X-ray analyses have been made for two crystalline modifications of the tricyclic orthoamide **1b**: a cubic trihydrate in space group *Pa*3 (Z = 8), where the molecule has crystallographic threefold rotation symmetry, and an anhydrous monoclinic form in space group $P2_1/c$ (Z = 8) where two symmetry-independent molecules have different configurations, one all-*trans* (as in the cubic trihydrate), the other *cis,cis,trans*. In the cubic trihydrate, each orthoamide molecule is attached to a triad of H_2O molecules by OH···N H-bonds. A remarkable feature of this structure is the nearly eclipsed conformation about the central C–CH_3 bond. In the anhydrous crystal, both types of molecule have the normal staggered orientation of their Me groups. The reversal of the Me orientation in the trihydrate is attributed to C–H···O H-bonding, which must be much stronger and more directionally specific than has been previously assumed.

Introduction. – Our interest in the tricyclic orthoamide **1b** was awakened by the unusual spectroscopic properties reported for the corresponding demethyl compound **1a**: in the ^{1}H-NMR spectrum the signal of the methine H-atom is shifted strongly upfield (δ, 2.25–2.31 ppm) [1][2], in the ^{13}C-NMR spectrum the central C–H bond has a remarkably low ^1J(C,H) coupling constant (*ca.* 140 Hz) [2], and the IR spectrum shows an abnormally low stretching frequency (*Bohlmann* band, 2450 cm^{-1}) [1][3]. All these features can be associated with the all-*trans*, all-chair configuration of **1a**, which places all three N lone pairs antiperiplanar (*app*) to the central C–H bond. Similarly, the ^{13}C-NMR spectrum of **1b** shows a remarkably high-field signal (δ(C) –4 ppm) for the methyl C-atom, again attributable to lone-pair orientation influences in the all-*trans* configuration [4].



1a R = H
1b R = CH_3

Here, we describe results of low-temperature X-ray analyses of crystalline **1b** and its trihydrate **1b** · $3H_2O$. A remarkable feature of the trihydrate structure is the nearly eclipsed orientation of the Me group with respect to the three central C–N bonds of the orthoamide molecule, which has the all-*trans* configuration inferred from the earlier spectroscopic results [4]. As the C–H bonds of the Me group point towards O-atoms of surrounding H_2O molecules in the crystal structure, we attribute this unprecedented eclipsed orientation of the Me group to the influence of C–H···O H-bonding. At any rate, it is not characteristic of the molecular structure itself, since it does not occur in the crystal of anhydrous **1b**. This crystal contains two independent sets of molecules, one with the all-*trans*, the other with the *cis,cis,trans* configuration. In both sets, the Me group adopts its normal staggered conformation about the central C–C bond. A preliminary account of this work has already appeared [5].

Experimental. – All our experiments were done with a small sample of **1b** prepared in Prof. *Gary Weisman*'s laboratory. The crystalline solid obtained by cooling this sample (liquid at r.t.) proved to be a cubic trihydrate. A crystal suitable for X-ray analysis (data set *I*) was obtained by slow cooling from about 305 to 290 K of a drop of liquid enclosed in a capillary mounted directly on the diffractometer. The crystal for data set *II* (anh., monoclinic) was obtained by distillation of the trihydrate over CaH_2, followed by slow cooling (from 293 to 280 K) of a drop of the distillate in a capillary mounted directly on the diffractometer.

The X-ray measurements were made on an *Enraf-Nonius CAD4* diffractometer equipped with graphite monochromator (Mo$K\alpha$ radiation, λ = 0.7107 Å) and a locally modified gas-stream low-temp. device. Temp. fluctuations as monitored with a Pt 100 Ω resistor were less than 0.5 K during the X-ray measurements. Relevant experimental details are summarized in *Table 1*. Unit-cell dimensions were derived by least-squares fitting of setting angles for 18 (data set *I*) and 22 (data set *II*) reflections with 2θ angles in the range 40 to 44°. For data set II, to reduce the effect of radiation damage on the intensity measurements, the reflection sphere was covered beginning at the outside and working inward in shells of diminishing radius[6][7]. One effect of radiation damage is to reduce the extinction error, which became noticeably less severe towards the end of the measurements.

Table 1. *Experimental Details of X-Ray Diffraction Measurements for the Cubic Trihydrate* (data set *I*) *and the Anhydrous Monoclinic Crystal* (data set *II*)

Data set	*I*	*II*
Temperature of data collection [K]	81	81
Melting point [K]	283–289	290–297
Approximate crystal dimensions [mm]	0.3x0.3x0.5	0.5x0.5x0.5
Space group	*Pa*3	$P2_1/c$
Cell dimensions *a* [Å]	13.719(3)	17.502(3)
b [Å]		8.537(2)
c [Å]		17.674(3)
β [°]		125.89(2)
Unit cell contents	$8 \times C_{11}H_{21}N_3 \cdot 3H_2O$	$8 \times C_{11}H_{21}N_3$
D_c [g/cm^3]	1.28	1.21
2 sin θ/λ range [Å^{-1}]	1.808	1.808
No. of symmetry equivalent orientations measured	3	2
No. of measured reflections	8094	27460
$R_{int} = (\sum_H \sum_N \mid I_{H,i} - \langle I_H \rangle \mid)/\sum_H N \langle I_H \rangle$	0.027	0.016
No. of unique reflections	2674	13234
No. of observed reflections ($I > 3\ \sigma(I)$)	1554	8627
No. of variables in final least-squares analysis	90	422
Type of refinement	*F*	*F*
Scan mode	ω/θ	ω/θ
Exponentially modified weight factor *r* [Å^2]	3.0	2.5
Extinction correction	isotropic	isotropic
$y = P/P_k$ for the strongest reflection	0.96	0.80–0.94[a])
$R(F)$	0.032	0.029
$R_w(F)$	0.031	0.035

[a]) The lower *y* value refers to observations near the beginning of the measurement, the larger to observations near the end.

The structures were solved by direct methods [8] and refined by full-matrix least-squares analysis [9]. All H-atoms were located from difference maps and assigned isotropic displacement parameters in the refinements; other atoms were refined with anisotropic displacement parameters. In particular, the location and refinement of the H-atoms of the Me groups presented no special difficulties.

Atomic positional coordinates and displacement parameters are listed for the cubic trihydrate in *Table 2* (molecule A) and for the anh. monoclinic crystal in *Table 3*, where the data for the two independent molecules B and C are tabulated separately. Bond lengths and angles for the three molecules are given in *Table 4*. The atomic numbering is shown in *Figs. 1* and *2*.

Table 2. *Positional Coordinates and Displacement Parameters* (e.s.d. in parentheses) *for the Atoms in the Cubic Trihydrate Crystal.* Coordinates for the complete set of atoms of the standard molecule A are related by the threefold symmetry axis of the space group: *x,y,z; z,x,y; y,z,x.* For the atomic numbering, see *Fig. 1.*

Atom	x	y	z	U^{11}(or U)	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O	0.39573(4)	0.40245(4)	0.60425(4)	0.0165(2)	0.0141(2)	0.0129(2)	–0.0028(2)	–0.0030(2)	–0.0005(2)
C(1)	0.32905(4)	0.32905	0.32905	0.0067(1)	0.0067	0.0067	–0.0004(2)	–0.0004	–0.0004
N(2)	0.31189(4)	0.31235(4)	0.43465(4)	0.0081(2)	0.0074(2)	0.0067(2)	0.0003(2)	0.0005(1)	0.0002(1)
C(3)	0.21159(5)	0.33651(5)	0.46471(5)	0.0088(2)	0.0113(2)	0.0103(2)	–0.0004(2)	0.0023(2)	–0.0002(2)
C(4)	0.19042(5)	0.44273(5)	0.44170(5)	0.0104(2)	0.0113(2)	0.0116(2)	0.0022(2)	0.0018(2)	–0.0015(2)
C(5)	0.33493(5)	0.21155(5)	0.46330(5)	0.0116(2)	0.0085(2)	0.0094(2)	–0.0002(2)	0.0000(2)	0.0018(2)
C(6)	0.26335(4)	0.26335	0.26335	0.0091(2)	0.0091	0.0091	–0.0016(2)	–0.0016	–0.0016
H(O)	0.379(1)	0.384(1)	0.545(1)	0.029(3)					
H(OO)	0.391(1)	0.467(1)	0.605(1)	0.057(6)					
H(31)	0.2096(9)	0.3240(9)	0.5354(9)	0.011(3)					
H(32)	0.1631(9)	0.2931(9)	0.4323(9)	0.013(3)					
H(41)	0.123(1)	0.4578(9)	0.4558(9)	0.013(3)					
H(42)	0.231(1)	0.484(1)	0.4837(9)	0.017(3)					
H(51)	0.3212(9)	0.2090(9)	0.5331(9)	0.009(3)					
H(52)	0.2921(9)	0.1642(9)	0.429(1)	0.017(3)					
H(6)	0.213(1)	0.227(1)	0.302(1)	0.020(3)					

Table 3. *Positional Coordinates and Displacement Parameters* (e.s.d. in parentheses) *for the Two Independent Molecules B* (above) *and C* (below) *in the Monoclinic Crystal.* For the atomic numbering, see *Fig. 2.*

Atom	x	y	z	U^{11}(or U)	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Molecule B									
C(1)	1.06183(3)	0.25956(5)	0.90317(3)	0.0085(1)	0.0084(1)	0.0083(1)	0.0002(1)	0.0050(1)	–0.0002(1)
N(2)	1.07223(3)	0.39869(5)	0.86038(3)	0.0112(1)	0.0078(1)	0.0127(2)	–0.0004(1)	0.0079(1)	0.0004(1)
C(3)	1.16979(4)	0.44226(6)	0.90135(4)	0.0132(2)	0.0125(2)	0.0168(2)	–0.0041(1)	0.0093(2)	–0.0023(2)
C(4)	1.22197(4)	0.30558(7)	0.89591(4)	0.0111(2)	0.0164(2)	0.0175(2)	–0.0016(1)	0.0093(2)	–0.0001(2)
C(5)	1.21093(4)	0.16045(6)	0.93857(4)	0.0090(2)	0.0154(2)	0.0151(2)	0.0013(1)	0.0069(2)	0.0017(2)
N(6)	1.11119(3)	0.12946(5)	0.89363(3)	0.0086(1)	0.0086(1)	0.0114(1)	0.0010(1)	0.0063(1)	0.0006(1)
C(7)	1.09760(4)	–0.02228(6)	0.92248(4)	0.0131(2)	0.0095(2)	0.0140(2)	0.0027(1)	0.0088(2)	0.0026(1)
C(8)	0.99324(4)	–0.06128(6)	0.86599(4)	0.0147(2)	0.0088(2)	0.0146(2)	–0.0013(1)	0.0096(2)	–0.0005(1)
C(9)	0.93917(3)	0.07299(6)	0.87039(4)	0.0109(2)	0.0104(2)	0.0128(2)	–0.0008(1)	0.0076(1)	0.0008(1)
N(10)	0.96030(3)	0.22017(5)	0.84422(3)	0.0078(1)	0.0086(1)	0.0103(1)	0.0006(1)	0.0052(1)	0.0010(1)
C(11)	0.90135(4)	0.34539(6)	0.84071(4)	0.0119(2)	0.0122(2)	0.0153(2)	0.0037(1)	0.0091(2)	0.0031(1)
C(12)	0.91493(4)	0.49401(6)	0.80275(4)	0.0156(2)	0.0118(2)	0.0177(2)	0.0049(1)	0.0109(2)	0.0048(2)
C(13)	1.01878(4)	0.53463(6)	0.85559(4)	0.0172(2)	0.0085(2)	0.0175(2)	0.0014(1)	0.0116(2)	0.0009(1)
C(14)	1.10079(4)	0.28798(6)	1.00692(3)	0.0136(2)	0.0144(2)	0.0094(2)	–0.0010(1)	0.0066(1)	–0.0019(1)
H(31)	1.1657(8)	0.533(1)	0.8648(8)	0.019(2)					
H(32)	1.2036(9)	0.483(1)	0.9668(9)	0.025(3)					
H(41)	1.2915(9)	0.332(1)	0.9289(9)	0.023(3)					
H(42)	1.1938(8)	0.282(1)	0.8280(9)	0.023(3)					
H(51)	1.2471(8)	0.174(1)	1.0083(8)	0.019(2)					
H(52)	1.2383(8)	0.068(1)	0.9290(8)	0.019(2)					
H(71)	1.1300(8)	–0.099(1)	0.9092(9)	0.022(3)					
H(72)	1.1262(8)	–0.028(1)	0.9907(8)	0.019(3)					

Table 3 (cont.)

Atom	x	y	z	U^{11}(or U)	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
H(81)	0.9836(8)	–0.156(1)	0.8902(8)	0.021(3)					
H(82)	0.9694(8)	–0.078(1)	0.8024(8)	0.016(2)					
H(91)	0.9512(8)	0.076(1)	0.9321(8)	0.017(2)					
H(92)	0.8691(8)	0.053(1)	0.8258(8)	0.021(3)					
H(111)	0.8368(8)	0.307(1)	0.8007(8)	0.019(2)					
H(112)	0.9124(8)	0.363(1)	0.9028(9)	0.024(3)					
H(121)	0.8896(8)	0.480(1)	0.7373(9)	0.025(3)					
H(122)	0.8820(8)	0.582(1)	0.8074(8)	0.021(3)					
H(131)	1.0440(9)	0.579(1)	0.9186(9)	0.022(3)					
H(132)	1.0279(8)	0.616(1)	0.8227(8)	0.019(2)					
H(141)	1.064(1)	0.367(2)	1.013(1)	0.039(4)					
H(142)	1.165(1)	0.322(2)	1.044(1)	0.037(3)					
H(143)	1.096(1)	0.197(2)	1.035(1)	0.035(3)					
Molecule C									
C(1)	0.57252(3)	0.30237(6)	0.68712(3)	0.0084(1)	0.0104(2)	0.0102(2)	0.0007(1)	0.0047(1)	0.0010(1)
N(2)	0.56533(3)	0.39040(5)	0.61151(3)	0.0133(2)	0.0127(2)	0.0111(2)	0.0032(1)	0.0074(1)	0.0029(1)
C(3)	0.55393(5)	0.28628(8)	0.53907(4)	0.0251(3)	0.0208(2)	0.0114(2)	0.0096(2)	0.0098(2)	0.0032(2)
C(4)	0.63209(6)	0.16329(8)	0.57878(5)	0.0318(3)	0.0231(3)	0.0159(2)	0.0139(2)	0.0151(2)	0.0037(2)
C(5)	0.63970(5)	0.07556(7)	0.65766(4)	0.0221(2)	0.0133(2)	0.0136(2)	0.0061(2)	0.0081(2)	0.0000(2)
N(6)	0.65065(3)	0.18424(5)	0.72751(3)	0.0119(2)	0.0102(1)	0.0104(1)	0.0028(1)	0.0058(1)	0.0017(1)
C(7)	0.66316(4)	0.09485(7)	0.80503(4)	0.0187(2)	0.0138(2)	0.0150(2)	0.0041(2)	0.0095(2)	0.0053(2)
C(8)	0.68064(5)	0.20362(8)	0.88192(4)	0.0230(2)	0.0225(2)	0.0129(2)	0.0088(2)	0.0105(2)	0.0063(2)
C(9)	0.60369(4)	0.32892(8)	0.84034(4)	0.0194(2)	0.0217(2)	0.0146(2)	0.0064(2)	0.0120(2)	0.0044(2)
N(10)	0.59120(3)	0.41173(5)	0.76073(3)	0.0102(1)	0.0125(1)	0.0108(1)	0.0009(1)	0.0063(1)	0.0000(1)
C(11)	0.67003(4)	0.51953(7)	0.79387(4)	0.0101(2)	0.0142(2)	0.0171(2)	–0.0006(1)	0.0063(2)	–0.0039(2)
C(12)	0.65200(4)	0.61475(7)	0.71264(5)	0.0144(2)	0.0113(2)	0.0278(3)	–0.0001(2)	0.0126(2)	0.0015(2)
C(13)	0.64179(4)	0.50211(7)	0.64125(4)	0.0153(2)	0.0157(2)	0.0219(2)	0.0039(2)	0.0135(2)	0.0067(2)
C(14)	0.47514(4)	0.22889(7)	0.64575(4)	0.0102(2)	0.0171(2)	0.0195(2)	–0.0029(2)	0.0058(2)	0.0001(2)
H(31)	0.4893(9)	0.231(1)	0.506(1)	0.029(3)					
H(32)	0.5531(9)	0.354(1)	0.4930(9)	0.027(3)					
H(41)	0.693(1)	0.212(2)	0.602(1)	0.035(3)					
H(42)	0.617(1)	0.092(2)	0.530(1)	0.036(3)					
H(51)	0.6947(9)	0.004(1)	0.6878(9)	0.026(3)					
H(52)	0.5826(9)	0.004(1)	0.6330(9)	0.029(3)					
H(71)	0.6091(9)	0.029(1)	0.7838(9)	0.024(3)					
H(72)	0.7179(9)	0.024(1)	0.8294(9)	0.025(3)					
H(81)	0.680(1)	0.145(1)	0.928(1)	0.033(3)					
H(82)	0.7419(9)	0.253(2)	0.9132(9)	0.032(3)					
H(91)	0.6192(9)	0.410(1)	0.8865(9)	0.028(3)					
H(92)	0.5429(9)	0.282(1)	0.8219(9)	0.026(3)					
H(111)	0.6732(8)	0.588(1)	0.8397(9)	0.022(3)					
H(112)	0.7323(8)	0.466(1)	0.8250(8)	0.017(2)					
H(121)	0.7052(9)	0.688(1)	0.734(1)	0.030(3)					
H(122)	0.5920(8)	0.679(1)	0.6826(8)	0.020(3)					
H(131)	0.7032(9)	0.452(1)	0.6680(9)	0.025(3)					
H(132)	0.6264(8)	0.558(1)	0.5864(8)	0.021(3)					
H(141)	0.4534(9)	0.161(1)	0.5930(9)	0.028(3)					
H(142)	0.4287(9)	0.312(1)	0.6267(9)	0.028(3)					
H(143)	0.4752(9)	0.166(1)	0.6925(9)	0.028(3)					

Table 4. *Bond Lengths* [Å] *and Angles* [°] *for the Three Independent Molecules.* For the atomic numbering, see *Figs. 1* (for molecule A) and *2* (for molecules B and C). E.s.d. are *ca.* 0.001 Å for the bond lengths and *ca.* 0.1° for the bond angles.

	Molecule A		Molecule A
C(1)–C(6)	1.561	N(2)–C(1)–C(6)	112.5
C(1)–N(2)	1.485	C(1)–N(2)–C(3)	112.7
N(2)–C(3)	1.474	N(2)–C(3)–C(4)	109.6
C(3)–C(4)	1.519	C(3)–C(4)–C(5)	110.0
C(4)–C(5)	1.519	C(4)–C(5)–N(2')	109.7
C(5)–N(2')	1.472	C(5)–N(2')–C(1)	111.8
		N(2)–C(1)–N(2')	106.3
		C(3)–N(2)–C(5')	109.7

	Molecule B	Molecule C		Molecule B	Molecule C
C(1)–C(14)	1.556	1.540	C(1)–N(2)–C(3)	114.3	112.1
C(1)–N(2)	1.476	1.473	N(2)–C(3)–C(4)	110.2	112.7
C(1)–N(6)	1.476	1.501	N(2)–C(1)–N(6)	106.9	110.1
C(1)–N(10)	1.478	1.474	N(2)–C(1)–N(10)	106.3	109.5
N(2)–C(3)	1.459	1.473	C(3)–C(4)–C(5)	109.8	109.5
N(2)–C(13)	1.462	1.467	C(4)–C(5)–N(6)	109.7	111.1
C(3)–C(4)	1.519	1.530	C(5)–N(6)–C(7)	111.0	109.4
C(4)–C(5)	1.521	1.518	C(5)–N(6)–C(1)	113.3	113.1
C(5)–N(6)	1.457	1.464	N(6)–C(7)–C(8)	110.1	111.0
N(6)–C(7)	1.462	1.468	N(6)–C(1)–N(10)	106.9	109.7
C(7)–C(8)	1.519	1.522	C(7)–C(8)–C(9)	110.3	109.8
C(8)–C(9)	1.517	1.529	C(7)–N(6)–C(1)	113.7	112.9
C(9)–N(10)	1.460	1.472	C(8)–C(9)–N(10)	110.6	113.0
N(10)–C(11)	1.462	1.465	C(9)–N(10)–C(11)	109.8	110.0
C(11)–C(12)	1.518	1.513	C(9)–N(10)–C(1)	113.3	111.8
C(12)–C(13)	1.519	1.511	N(10)–C(11)–C(12)	109.9	109.5
			C(11)–N(10)–C(1)	113.0	114.9
			C(11)–C(12)–C(13)	111.1	107.9
			C(12)–C(13)–N(2)	110.4	110.5
			C(13)–N(2)–C(3)	110.4	109.5
			C(13)–N(2)–C(1)	113.7	115.6
			C(14)–C(1)–N(2)	112.2	107.2
			C(14)–C(1)–N(6)	111.7	113.5
			C(14)–C(1)–N(10)	112.4	106.8

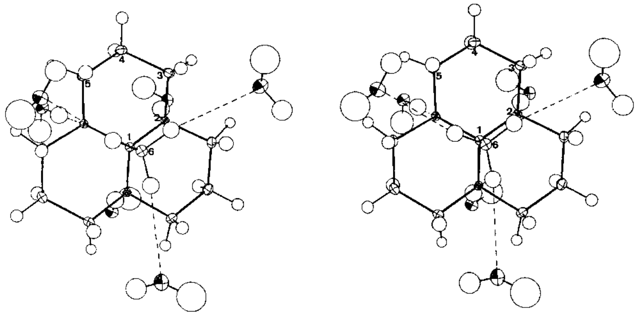


Fig. 1. *Stereoview of molecule A with atomic numbering.* Equiprobability ellipsoids are drawn at the 50% probability level. Note the six attached H_2O molecules and the nearly eclipsed conformation about the Me group.

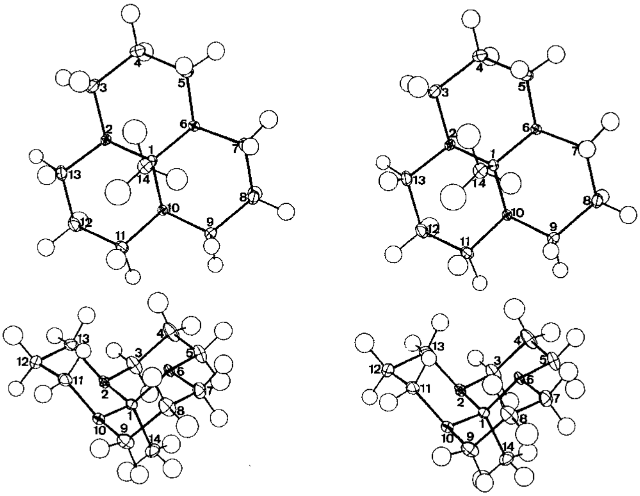


Fig. 2. *Stereoview of molecules B* (all-*trans* configuration, above) *and C* (*cis,cis,trans* configuration, below) *with atomic numbering*. Equiprobability ellipsoids are drawn at the 50% probability level.

ADP Analyses. – Analysis of the anisotropic atomic displacement parameters (ADP's) listed in *Tables 1* and *2* with the program THMA 11 [10] shows that the observed U^{ij} values are reasonably compatible with rigid-body behaviour [11] for all three molecules. The values for the N-atoms tend to be slightly lower than the others (by about 10×10^{-4} Å^2, but it is not clear whether this is a real effect or due to some inadequacy of the model used to fit the data in the least-squares refinements (*e.g.*, neglect of deformation density in the least-squares model). The analysis of the ADP's in terms of molecular **T**, **L**, and **S** tensors [10][12] indicates that the rigid-body translational motions are fairly isotropic (within 10% for the all-*trans* molecules A and B, and within 20% for the *cis,cis,trans* molecule C). There is nothing specially noteworthy about the librational tensors either; they are quite small, and so, therefore, are the librational motion corrections [13] to the bond lengths (the values given in *Table 4* are uncorrected). The largest eigenvalue of **L** for any of the three molecules is 11 deg^2, for molecule C, and not about an axis with any obvious relationship to the inertial axes.

In a separate analysis of the monoclinic crystal at a temperature within a degree or two of the melting point (details not given here), the atomic parameters of both molecules could be satisfactorily refined – somewhat to our surprise! The large eigenvalue of **L** for molecule C increased to about 40 deg^2, *i.e.*, *ca.* 3.6 times the value at low temperature or roughly by the ratio of the temperatures.

Discussion of the Structures. – Molecule A, in the trihydrate crystal, shows a remarkable structural feature: as can be seen from *Fig. 1*, the conformation about the central C–C bond is nearly eclipsed with N–C–C–H torsion angle of 8.2(9)°. This cannot be an intrinsic property of the molecule, since the usual staggered conformation is found for the corresponding bond in the closely similar molecule B in the anhydrous crystal (*Fig. 2*). We believe that it is a result of directed C–H···O H-bonding with the particular arrangement of H_2O molecules that occurs in the cubic trihydrate crystal structure .

As seen in *Figs. 1* and *3*, each N-atom of the tricyclic orthoamide molecule is involved in H-bonding to a H_2O molecule (O···N, 2.874 Å; O–H···N angle, 161°). The H_2O molecules then make additional H-bonds among themselves in such a way that the two triads related by the crystallographic inversion centre form a chair-like $(H_2O)_6$ ring (O···O, 2.770 Å; O–H···O angle, 172°; O···O···O angle, 91.2°). H-bonded dimeric units, elongated along the body diagonals of the cubic unit cell, are thus formed, as illustrated in *Fig. 3*. Similar chair-like rings of H_2O molecules are known to occur elsewhere, for example, in ice II [14] and in the crystalline trihydrate of 2,4,6-trimethyl-1,3,5-triazacyclohexane [15]. For the H_2O molecules themselves, the coordinates in *Table 2* lead to O–H distances of 0.88(2) and 0.89(2) Å, characteristically *ca.* 0.1 Å too short. The H–O–H angle is 106.1°.

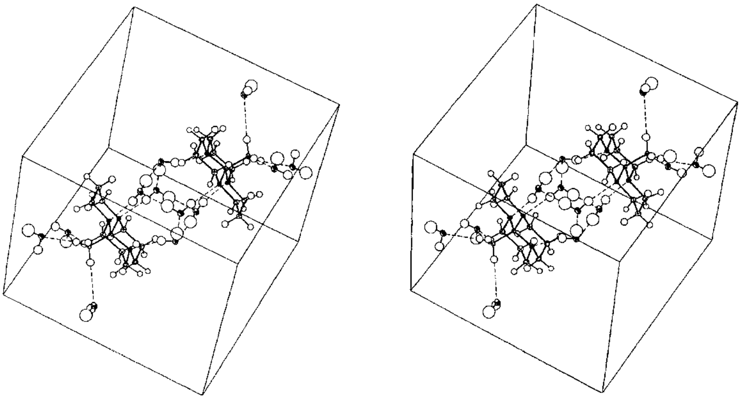


Fig. 3. *Stereoview of part of the three-dimensional network of interlinked orthoamide and H_2O molecules in the cubic trihydrate crystal structure.* Note the centrosymmetric $(H_2O)_6$ chair-like ring at the centre of the pattern and the threefold rotation axis along the body diagonal.

On the other side of the tricyclic orthoamide, each C–H bond of the Me group points nearly at an O-atom of a neighbouring triad of H_2O molecules (H···O, 2.65 Å, C–H···O angle, 170°). If the observed C–H distance of *ca.* 1.00 Å is adjusted upward to correct for the characteristic X-ray shortening effect, the H···O distance in question decreases by *ca.* 0.1 Å. The nearly linear angle is highly suggestive, and, while the corrected distance may be somewhat on the long side for C–H···O H-bonding [16][17], it still lies well within the range found in other structures [18]. Moreover, while the N–C–C–H torsion angle is 8.2°, the N–C–C···O torsion angle is only 0.9°. These indications all seem to support the idea that C–H···O H-bonding is largely responsible for the unprecedented Me conformation in molecule A.

Table 4 lists bond lengths and angles for the three independent molecules of the cyclic orthoamide and reveals some interesting similarities and differences. All three molecules show effective higher symmetry than that imposed crystallographically; thus the two all-*trans* molecules A and B show effective $C_{3v}(3m)$ symmetry, and the *cis,cis,trans* molecule C also shows effective mirror symmetry, the highest possible compatible with its structure and configuration.

The main differences between the two all-*trans* molecules A and B are: the central $C–CH_3$ bond is longer in A, 1.561 *vs.* 1.556 Å, and so are the C–N bonds, 1.486 *vs.* 1.477 Å for the type C(1)–N(2), and 1.474 *vs.* 1.460 Å for the type C(3)–N(2). The estimated standard deviations in the bond lengths are *ca.* 0.001 Å, and the differences are much too large to be attributed to motional errors (see section on ADP analyses). The longer C–N bond lengths in the trihydrate can be explained as a result of the incipient protonation of the N lone pairs engaged in H-bonding. Another effect of the incipient protonation is to increase slightly the degree of pyramidality at the N-atoms in the trihydrate. This is seen by comparing the sum of the three bond angles around the N-atoms in A (334.2°) and B (337.5° average). Insofar as H-bonding must weaken the stereoelectronic effect of the three *app* lone pairs on the C–CH_3 bond, the slightly longer bond length in the trihydrate has then to be attributed to the effect of eclipsing.

In molecule C, the central C–CH_3 bond is antiperiplanar (*app*) to one N lone pair and synclinal (*sc*) to two; the bond length (1.540 Å) is 0.016 Å shorter than in molecule B with three *app* interactions. However, perhaps the most striking structural expression of the stereoelectronic effect of lone pairs is the marked lengthening of the C(1)–N(6) bond (1.501 Å) in molecule C, *app* to two N lone pairs, compared with C(1)–N(2) and C(1)–N(10) (1.473 and 1.474 Å), *app* to other N–C bonds. This difference of 0.027 Å between constitutionally equivalent, conformationally different bonds is similar to that found in other molecules where comparable stereoelectronic effects are expected to be important [19][20]. Bond-length differences of this magnitude may be associated with significant differences in chemical reactivity of the respective bonds [21]. Indeed, it seems likely that the transformation of protonated **1a** [22] and **1b** [23] to the corresponding bicyclic guanidinium cations (involving fission of one of the three central C–N bonds) proceeds *via* the *cis,cis,trans* configuration. It is also noteworthy that the two longest C–C bonds in the *cis,cis,trans* tricyclic system are those parallel to the long C–N bond, *i.e.*, the two that are each *app* to one N lone pair.

A stereoview of the anhydrous monoclinic crystal structure is shown in *Fig. 4*. At the centre of the box, a double layer of *cis,cis,trans* molecules extends in the plane containing the **b** and **c** axes. The C–CH_3 bonds point nearly along ±**a***, into the middle of the double layers, and these are interleaved with single layers of all-*trans* molecules with their C–CH_3 bonds pointing nearly along ±**c***.

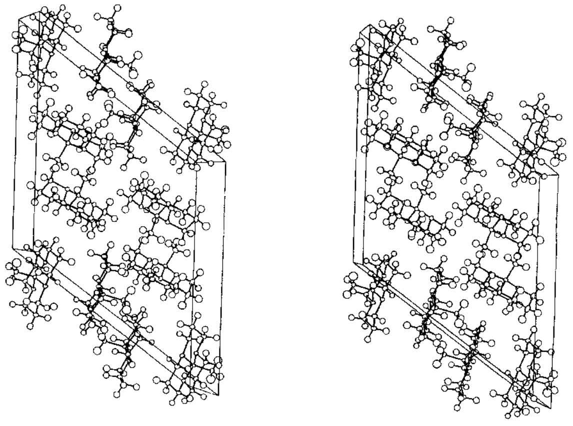


Fig. 4. *Stereoview of the anhydrous monoclinic crystal structure, viewed nearly along the direction of the* b *axis* (*a* axis vertical), *showing double layers of* cis,cis,trans *molecules interleaved with single layers of all-*trans *molecules*

Difference Maps. – As a test of the quality of the diffraction data, we have calculated electron-density difference maps for several sections of the anhydrous structure. (With the available computer programs, it was more difficult to obtain the corresponding maps for the cubic crystal.) The maps, shown in *Figs. 5, 6,* and *7*, were calculated with 4840 reflections with $I > 5\sigma(I)$ within a $2\sin\theta/\lambda$ radius of 1.4 Å^{-1} (80% of all measured reflections within this limiting radius). They have a low noise level and show well defined peaks of approximately 0.4 e · Å^{-3} close to the midpoints of all C–C bonds and slightly lower ones of *ca.* 0.3 e · Å^{-3} close to the midpoints of the C–N bonds. Peaks of approximately this height also occur *ca.* 0.6 Å from the N-atoms in the lone-pair directions (see *Fig. 7* for an example). The shapes, heights, and positions of lone-pair peaks are much more sensitive to the high-order cut-off than are those of bond peaks [24]. Otherwise the maps are practically featureless.

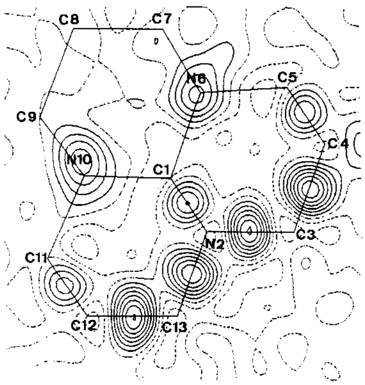


Fig. 5. *Molecule B. Electron-density difference map in the plane passing through C(13),N(2),C(3).* This plane lies very close to the positions of C(12) and C(4) and also cuts through the lone-pair density peaks of N(6) and N(10). Contour intervals are at 0.05 e · Å^{-3}. The corresponding maps through the planes C(5),N(6),C(7) and C(9),N(10),C(11), related by the approximate C_{3v} molecular symmetry, are very similar.

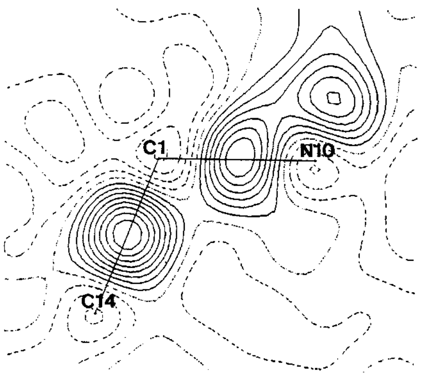


Fig. 6. *Molecule B. Electron-density difference map in the plane passing through C(14),C(1),N(10) showing the N lone-pair density peak of N(10).* Contour intervals are at 0.05 e · Å^{-3}. The corresponding maps through the planes C(14),C(1), N(2) and C(14),C(1),N(6), related by the approximate C_{3v} molecular symmetry, are very similar.

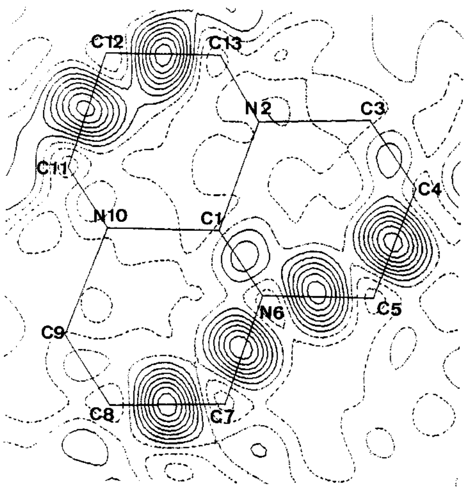


Fig. 7. *Molecule C. Electron-density difference map in the plane passing through C(5),N(6),C(7).* This plane lies very close to the positions of C(4), C(8), C(11), C(12), C(13) (see *Fig. 2*). Atoms N(6), C(1), C(12) lie in the (non-crystallographic) molecular mirror plane. Contour intervals are at 0.05 e · Å^{-3}.

General Implications. – From the structural evidence described here, it seems likely that the eclipsed conformation of the C–CH$_3$ bond in the cubic trihydrate crystal is due to C–H···O H-bonding. There is no reason to believe that the rotation barrier is inverted or even reduced in the cyclic orthoamide molecule. On the contrary, preliminary calculations for ethane-1,1,1-triamine (lone pairs *app* to the C–C bond), a model of the free molecule, suggest that the stable conformation is staggered with a barrier of the order of 5.5 kcal · mol^{-1}, *i.e.*, somewhat higher than in ethane [5]. This suggests, in turn, that the energy associated with each of the C–H···O H-bonds per molecule in the cubic crystal must be at least 1.8 kcal · mol^{-1}, far in excess of current estimates based on calculated CH$_4$···OH$_2$ interaction energies. New investigations in progress [5][25] suggest that high-order cooperative effects (*e.g.*, CH$_4$···O(H)H···NH$_3$) may play an important role in raising the interaction energy to the required level.

The fact that a suitable arrangement of H$_2$O molecules can invert the rotation barrier of a Me group through H-bonding has obvious implications for interactions between 'hydrophobic' regions of molecules and aqueous environments. The H$_2$O molecule arrangements will, in general, be determined by the directional properties of the stronger O–H···O and N–H···O H-bonds. This arrangement, in turn, may affect the conformation of aliphatic chains, *etc.*, through the formation of weaker, but still direction specific, C–H···O bonds. Hence, conformational regularities observed for aliphatic portions of molecules in non-aqueous environments may not be applicable without reservations when the molecules are embedded in a matrix of H$_2$O molecules.

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